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Behavioral change，physiological modification，and metabolic detoxification：mechanisms of insecticide resistance

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Abstract：Insecticide resistance is"the development of an ability in a strain of some organisms to tolerate doses of a toxicant which would prove lethal to a majority of individuals in a normal population of the same species". Mechanisms of resistance，such as behavioral change，physiological modification or metabolic detoxification，decrease the effective dose available at the target site. Behavioral resistance is defined as any behavior that reduces an insect's exposure to toxic compounds or that allows an insect to survive in an environment that is harmful and/or fatal to the majority of insects. Physiological modification mechanisms permit insects to survive lethal doses of a toxicant through decreased penetration of insecticides，increased sequestration/storage of insecticides，and accelerated excretion of insecticides. Metabolic detoxification is conferred by cytochrome P450 monooxygenases (cytochrome P450s)，hydrolases，and glutathione transferases (GSTs). Cytochrome P450s constitute the largest gene superfamily and are critical for the detoxification and/or activation of xenobiotics and the metabolism of endogenous compounds. Increased P450-mediated detoxification has been found in many insect species，resulting in enhanced insecticide resistance. Glutathione transferases (GSTs) are soluble dimeric proteins involved in the metabolism，detoxification，and excretion of a large number of endogenous and exogenous compounds. Elevated GST activities have been implicated in resistance in many insect species. Hydrolases or esterases，a group of heterogeneous enzymes，have been identified as the active agents promoting hydrolase-mediated resistance that protect insects by either binding and sequestering insecticides through overproduction of proteins，or enhancing the metabolism of insecticides through increased enzyme activities.

Key words：Insecticide resistance；behavioral change；physiological modification；metabolic detoxification；glutathione S-transferases；cytochrome P450

1 INTRODUCTION

Resistance has been defined as"the development of an ability in a strain of some organisms to tolerate doses of a toxicant which would prove lethal to the majority of individuals in a normal population of the same species"(WHO，1957). Resistance is a pre-adaptive phenomenon，so that even before exposure to a pesticide，some individuals already have appropriate factors that allow them to survive (Brown and Pal，1971). Resistance is inherited and survivors can pass the resistance gene(s) to their offspring (WHO，1957).

Following the first case of DDT resistance in 1946 (Georghiou and Mellon，1983)，insecticide resistance has developed at a rapid pace. Insecticide resistance has now occurred in all five major classes of pesticides (DDT and its analogues，cyclodienes，carbamates，organophosphates，and pyrethroids) (Georghiou，1986)，as well as in some relatively new insecticides，such as abamectin (Scott，1989)，Bacillus thuringiensis (Tabashnik *et al*.，2000)，imidacloprid (Liu and Yue，2000；Wei *et al*.，2001；Pan *et al*.，2003)，spinosad (Moulton *et al*.，2000)，and fipronil (Liu and Yue，2000). Nearly all the economically important insect species have developed resistance to at least one insecticide (Georghiou and Lagunes-Tejeda，1991) and some species have developed resistance to more than one class of insecticide (Georghiou，1980；Leng *et al*.，1996). Resistance has resulted in the need for increased dosage and frequency of application，increased cost，environmental contamination，and disruption of wildlife and biological control agents (Scott，1991). Resistance has also caused outbreaks of human diseases when insect vectors could not be controlled (Hemingway and Ranson，2000).

Mechanisms of resistance，such as behavioral change，physiological modification or metabolic detoxification，have contributed to decreasing the

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effective dose delivered at the target site, whereas decreased target site sensitivity, such as altered sodium channels, acetylcholinesterase, and GABA receptor insensitivity, have contributed to rendering the dose that does arrive ineffective (Feyereisen, 1995; Tang and Bi, 1996; Chris *et al*. 2004; Ffrench-Constant *et al*., 2004; French-constant *et al*., 2004; Bues *et al*., 2005). In this review, we will focus on the mechanisms that decrease the effective dose that is available at the insects' target sites.

2 BEHAVIORAL RESISTANCE

Behavioral resistance is defined as the development of behaviors that reduce an insect's exposure to toxic compounds or that allow an insect to survive in an environment that is harmful and/or fatal to the majority of insects of the same species (Sparks *et al*., 1989). This can be divided into stimulus-dependent (required sensory stimulation) and stimulus-independent (does not require sensory stimulation) mechanisms (Georghiou, 1972). Stimulus-dependent behavioral resistance includes both irritability, in which an insect is stimulated to leave the immediate toxic environment upon contact with a treated surface, and repellency, in which an insect is stimulated to leave the immediate toxic environment before contact with a treated surface.

Behavioral resistance to insecticides has been documented in the horn fly, *Haematobia irritans* (L.) (Lockwood *et al*., 1985), where the resistant population was significantly more repelled and irritated by fenvalerate and permethrin than the susceptible population. In the subsequent dose-response tests, it was demonstrated that the resistant strain of horn flies exhibited a unique behavioral response pattern to four pyrethroids and DDT. Ross (1992) identified behavioral resistance in the German cockroach against pyrethroids, reporting that a decreased dispersal response occurred in the resistant strain compared with the susceptible strain. The existence of behavioral resistance in the German cockroach has been linked to a food component in the bait formulation of hydramethylnon (Silverman and Bieman, 1993). Initially, in 1983, a population of a field collected German cockroach strain was reduced by over 90% using glucose diets containing the insecticide hydramethylnon. By 1988, however, the survival rate had increased to 39%. The removal of glucose from their diets resulted in the survival rate of the population once again falling. Based on these findings, it has been suggested that the cockroaches had developed an aversion to the glucose in the toxicant/diet mixture (Silverman and Bieman, 1993). This is the first report of nutrient avoidance as a behavioral resistance mechanism. German cockroaches have also evolved behavioral resistance to a chlorpyrifos-based commercial bait (Ross, 1997), where the resistance to the bait was caused by an aversion to chlorpyrifos (Ross, 1998). Behavioral resistance in mosquitoes has been found to reduce the rate of mosquito entry into houses, increase the rate of early exit from houses and induce a change in biting times (Mbogo *et al*., 1996; Mathenge *et al*., 2001).

3 PHYSIOLOGICAL RESISTANCE MECHANISMS

Mankind has always faced competition from insects. With the advent of modern insecticides, mankind has been able to exert substantial control over many insect pests (Scott, 1991). Nevertheless, insects have developed physiological modification mechanisms that decrease penetration, increase sequestration/storage, and accelerate excretion of insecticides as the insects are exposed to them.

3.1 Decreased penetration/absorption

Many insecticides must pass through the insect cuticle in order to reach the site of action before lethal effects can occur. Decreased penetration has been found in a number of resistant strains of insects, such as the house fly, *Musca domestica* (L.) (Plapp and Hoyer, 1968; DeVries and Georghiou, 1981; Scott and Georghiou, 1986a, 1986b; Wen and Scott, 1999), the beet armyworm, *Spodoptera exigua* (Hübner) (Liu and Shen, 2003) and the German cockroach, *Blattella germanica* (L.) (Anspaugh *et al*., 1994; Wu *et al*., 1998; Valles *et al*., 2000). The gene causing this resistance has been named *pen* (Farnham, 1973). By itself, pen confers only a 2- to 3- fold resistance (Plapp and Hoyer, 1968; Sawicki, 1970), but it also acts as an enhancer for the resistance conferred by other mechanisms (Sawicki, 1970; Georghiou, 1971, 1986; Oppenoorth, 1985; Scott, 1991). The molecular basis for this mechanism is not clear, although it should be noted that although the cuticle is the major barrier, virtually any membrane has the potential to serve as a penetration barrier and therefore act as a resistance mechanism (Scott, 1991). For example, the peritrophic membrane can serve as a barrier preventing *Bacillus thuringiensis* toxin reaching the midgut brush border in lepidopterous larvae (Granados *et al*., 2001).

3.2 Increased sequestration/storage

Sequestration/storage as a resistance mechanism has been reported in several species of insects. For example, carboxylesterase E4, the enzyme that catalyzes the hydrolysis of organophosphates (OPs) and carbamates in the peach-potato aphid, *Myzus persicae* (Sulzer), shows relatively low catalytic activity towards insecticides by enzyme kinetic analysis. However, it is produced in very large quantities, accounting for approximately 3% of the total protein in highly resistant aphids. Therefore, it has been suggested that the resistance effect caused by E4 is not mediated by hydrolysis, but by storage/sequestration of a substantial proportion of a toxic dose of insecticides (Devonshire and Moores, 1982). Another example is carboxylesterase A2 from *Culex quinquefasciatus* (Say), where the major role of carboxylesterase A2 is to sequestrate the organophosphate insecticide (Ketterman *et al*., 1992). Similarly, esterase B2 from *Culex quinquefasciatus* (Say) also has a sequestration role in insecticide resistance (Karunaratne *et al*., 1993). Storage as a mechanism of resistance has also been reported in *Culex pipiens* (L.), in which an overproduction of esterases B1 was found to confer resistance to organophosphates through sequestration rather than metabolism (Cuany *et al*., 1993). Resistance caused by esterase sequestration of insecticide molecules also occurs in the rice stem borer, *Chilo suppressalis* (Walker) (Konno and Shishido, 1989), rice brown planthoppers, *Nilaparvata lugens* (Stål) (Chen and Sun, 1994), cotton bollworm, *Helicoverpa armigera* (Hübner) (Gunning *et al*., 1996), Colorado potato beetle, *Leptinotarsa decemlineata* (Say) (Lee and Clark, 1996; 1998), German cockroach, *Blattella germanica* (L.) (Prabhakaran and Kamble, 1995; Scharf *et al*., 1997), mosquito, *Culex tritaeniorhynchus* (Giles) (Karunaratne and Hemingway, 2000), and Australian sheep blowfly, *Lucilia cuprina* (Wiedemann) (Chen *et al*., 2001). In addition to esterase, glutathione S-transferase also offers protection against pyrethroid insecticides by binding to their molecules in a sequestering manner (Kostaropoulos *et al*., 2001).

3.3 Accelerated excretion

Accelerated excretion is another mechanism that is often involved in insecticide resistance. A wide variety of insect species have developed resistance to insecticides through this mechanism. For instance, in diazinon resistant thrips, *Frankliniella occidentalis* (Pergande), the diazinon excretion was faster than in a susceptible strain (Zhao *et al*., 1994). It has also been found that the resistance mechanism of Colorado potato beetles to azinphosmethyl may be potentiated by the generally rapid excretion of aziophosmethyl (Argentine *et al*., 1995). Compared with those from a susceptible strain, levels of excretion of cypermethrin were higher in larvae of field collecting tobacco budworms (Ottea *et al*., 1995). An increased excretion rate was also observed in the carbaryl-resistant populations of Western corn rootworm *Diabrotica virgifera virgifera* (LeConte) (Scharf *et al*., 1999).

4 METABOLIC DETOXIFICATION

Increased metabolic detoxification is one of the most common mechanisms of insecticide resistance (Hemingway and Karunaratne, 1998; Hemingway, 2000; Hemingway *et al*., 2004). Insects possess enzymes that protect them from xenobiotics, so it is not surprising that metabolic detoxification might be the most common mechanism of resistance to insecticides (Scott, 1991; Natsuhara *et al*., 2004). Overall, the metabolism of xenobiotics is a single or multi-step process in which lipophilic compounds are converted into more water-soluble metabolites, which can be readily excreted by a water-based excretory system. Oxidases, hydrolases, and glutathione-S-transferase are three major types of enzymes that are involved in the metabolic detoxification process.

4.1 Cytochrome P450-mediated detoxification

Although two primary types of oxidases, cytochrome P450 microsomal monoxoxygenases and flavin monooxygases, are commonly recognized, in insects only the former have so far been identified (Scott, 1991). Insect cytochrome P450 monooxgenases are known to be involved in the detoxification of both insecticides and plant toxins (Scott *et al*., 1998; Feyereisen, 1999). Insect cytochrome P450s are also involved in the biosynthesis and metabolism of insect hormones such as juvenile hormones and ecdysteroids, which are very important for insect growth, development, and reproduction (Feyereisen, 1999; Scott and Wen, 2001). They also play an important role in the adaptation of insects to their host plants. The role of monooxygenases in insecticide resistance first became apparent in the early 1960s when it was reported that the resistance of house flies to carbaryl could be eliminated by the P450 inhibitor sesamex (Eldefrawi *et al*., 1960). Since then, the evidence supporting monooxygenase mediated resistance has accumulated rapidly. Cytochrome P450 monooxygenase mediated detoxification is a very important resistance mechanism because it not only confers high levels of resistance (Scott and Georghiou, 1986a; Yang *et al*., 2004), but also provides cross resistance to unrelated compounds due to the wide variety of substrates that the P450 monooxygenases can metabolize (Scott, 1991).

Cytochrome P450s are one of the largest super gene families. To date, more than 500 P450 genes have been identified and named from various insects (http://drnelson.utmem.edu/P450.stats.all.htm). Some of these P450s that have been identified are found in insecticide resistant strains, and their association with resistance has been investigated. The first insect P450 gene to be cloned, *CYP6A1*, came from a diazinon resistant house fly strain, Rutgers (Feyereisen *et al*., 1989). *CYP6A1* was expressed at about 10-fold higher levels in Rutgers than in susceptible strains, and this elevated *CYP6A1* expression was proven to be not due to gene amplification (Carino *et al*., 1994). *CYP6A1* was mapped to autosome 5, and the factors responsible for the increased expression level were linked to autosome 2 (Feyereisen *et al*., 1995). This indicated that the expression of *CYP6A1* was regulated by trans-factors. *CYP6D1*, another P450 gene isolated from a house fly resistant strain, in this case Learn Pyrethroid Resistant (LPR) (Wheelock and Scott, 1989), was expressed at about a 10-fold higher level in LPR than in the susceptible strain (Tomita and Scott, 1995). It has been shown that the increased expression of *CYP6D1* in the LPR strain is due to an increased rate of transcription (Liu and Scott, 1998), which is regulated by factors on autosomes 1 and 2 (Liu and Scott, 1996). *CYP6G1* from *Drosophila melanogaster* was identified by the presence of a transposable element at the 5' end of the gene (Daborn *et al*., 2002). This gene was overexpressed in 28 strains of DDT-resistant *Drosophila melanogaster* collected throughout the world (Daborn *et al*., 2004). Transgenic analysis indicated that overtranscription of *CYP6G1* alone was necessary and sufficient for DDT resistance to develop (Daborn *et al*., 2002).

The overexpression of P450 genes in resistant insect strains is a common phenomenon. *CYP6A2* was expressed 20- to 30-fold higher in a malathion-resistant strain (91-R) of the fruit fly, *Drosophila melanogaster*, than a susceptible strain (Waters *et al*., 1992). *CYP4G8*, a P450 gene in Australian cotton bollworm, *Helicoverpa armigera* (Hubner), showed a 2-fold higher level in a pyrethroid resistant strain compared with a susceptible strain (Pittendrigh *et al*., 1997). *CYP6F1* from the southern house mosquito, *Culex quinquefasciatus* (Say), was expressed at a level 3-fold higher in a permethrinresistant strain than in the susceptible strain (Kasai *et al*., 2000). In malaria mosquitos, *Anopheles gambiae*, an adult-specific P450 gene, *CYP6Z1*, was expressed approximately11- and 4.5-fold higher in males and females, respectively, from a pyrethroid-resistant strain compared with individuals from a susceptible strain (Nikou *et al*., 2003). The expression of *CYP4G19* in the pyrethroid-resistant strain of the German cockroach was about 1.7-fold higher in the nymphs and approximately 5-fold higher in the adults compared with a susceptible strain (Pridgeon *et al*., 2003).

Nevertheless, overexpression of P450s in resistant strains may not be the sole determinant of their importance in resistance. It has been suggested that for a P450 to be involved in resistance, it must meet the following two criteria: 1) it must be shown to metabolize/sequester the compound to which the strain has monooxygenase-mediated resistance, and 2) its enzymes in the resistant strain must either express more or have a greater catalytic activity compared with those in a susceptible strain (Scott *et al*., 1998).

4.2 Hydrolase-mediated detoxification

Hydrolases or esterases represent many of the enzymes present in most organisms, including carboxylesterases and phosphorotriester hydrolases (Scott, 1991). Hydrolases are involved in the metabolism of OPs, carbamates, pyrethroids, and juvenile hormones (Oppenoorth, 1985; Scott, 1999). Although organophosphate (OP), carbamate, and pyrethroid insecticides are all substrates of hydrolases, hydrolase- mediated insecticide resistance has mainly been found for OPs and carbamates (Hemingway *et al*., 2004). The mechanisms of hydrolase-mediated insecticide resistance can usually be divided into two groups: elevated and non-elevated esterase-base mechanisms. Gene amplification of elevated esterases, resulting in the production of abundant proteins in resistant insects, has been identified as the primary mechanism of hydrolase-mediated resistance (Hemingway and Karunaratne, 1998; Small and Hemingway, 2000), protecting insects by binding and sequestering insecticides. However, non-elevated esterase-mediated resistance has also been identified in some insects and attributed to the enhanced metabolism of insecticides due to increased activities of the esterases (Ziegler *et al*., 1987; Whyard *et al*., 1995; Guo and Gao, 2005).

The correlation between non-elevated esterase-base mechanism and OP resistance was initially identified in OP-resistant house flies (van Asperen and Oppenoorth, 1959). Subsequently, this correlation was elucidated as the " mutant ali-esterase hypothesis ", where the resistant mutants were thought to gain the ability to hydrolyze OP substrates through a mutation in the major ali-esterase (carboxylesterase), while their ability to hydrolyze carboxylesterase substrates was reduced. This hypothesis proved to be accurate for the sheep blowfly *Lucilia cuprina* (Newcomb *et al*., 1997a), where a single amino acid substitution (glycine 137 to aspartic acid) of the ali-esterase E3 encoded by *LcαE7* gene lies within the active site of the enzyme and is responsible for both the loss of carboxylesterase activity and the acquisition of a novel OP hydrolase activity (Newcomb *et al*., 1997b). The same amino acid replacement has been documented in the OP-resistant house fly *Momusca domestica* (Claudianos *et al*., 1999). Another point mutation (tryptophan 251 to leucine) in the ali-esterase E3 has also been reported to be associated with malathion resistance in the sheep blowfly (Campbell *et al*., 1998). Lower esterase activity was also demonstrated in the OP-resistant blowfly, *Chrysomya putoria* (Wiedemann) (Townsend and Busvine, 1969) and the parasitoid *Habrobracon hebetor* (Say) (Perez-Mendoza *et al*., 2000).

In an elevated esterase-based mechanism, the overproduced esterase raised by gene amplification

（Hemingway，2000） quickly sequesters the OP insecticide with low hydrolysis activity （Claudianos *et al*.，1999）. For instance，carboxylesterase E4 was showed to overproduce in very large quantities （about 3% of the total protein） in the highly OP-resistant peach-potato aphid，*Myzus persicae* （Sulzer），and acting like a sponge to sequester insecticides （Devonshire *et al*.，1998） and accompanied by low E4 catalytic activity. This suggests that the resistance created by E4 is not conferred by hydrolysis，but rather by sequestration （Devonshire and Moores，1982）. The same mechanism has also been found in the mosquito *Culex pipiens* and *quinquefasciatus* （Raymond *et al*.，1998；Ferrari and Georghiou，1990；Small *et al*.，1998），the greenbug *Shizaphis graminum* （Gao and Zhu，2000），the tobacco budworm *Heliothis virescens* （Goh *et al*.，1995），and the brown planthopper *Nilaparvata lugens* （Vontas *et al*.，2000）.

4.3 Glutathione S-transferase-mediated detoxification

Glutathione S-transferases （GSTs） are a ubiquitous class of enzymes with a broad range of substrate specificities，which allows them to play a significant role in detoxification of a wide range of xenobiotics，including insecticides （Salinas and Wong，1999）. GSTs are normally involved in the conjugation of xenobiotics with endogenous substrates，such as glutathione. In insects，studies of GSTs have focused on their role in detoxifying foreign compounds，especially insecticides and plant toxins （Fournier *et al*.，1992；Ranson *et al*.，2001）. To date，6 different classes of GSTs，Delta，Sigma，Epsilon，Omega，Theta，and Zeta，have been identified in insects （Enayati *et al*.，2005）.

Elevated levels of GST activities have been associated with insecticide resistance to all the major classes of insecticides （Enayati *et al*.，2005；Sonoda and Tsumuki，2005）. In the cases that have been extensively studied，resistance or elevated levels of GST activities have been attributed to the overproduction of GST enzymes，which may result from either gene amplification or increases in transcriptional rate （Grant and Hammock，1992；Ranson *et al*.，2001）. Increased rates of DDT-dehydrochlorination catalyzed by GSTs confer resistance to DDT in many insect species，including mosquitoes *Aedes aegypti* （Grant *et al*.，1991），*Anopheles gambiae* （Prapanthadara *et al*.，1993） and *Anopheles dirus* （Prapanthadara *et al*.，1996；）. A cluster of eight GSTs genes have been identified in the Epsilon class from *Anopheles gambiae* （Ortelli *et al*.，2003；Enayati *et al*.，2005）. Some of these are overexpressed in a DDT-resistant *Anopheles gambiae* strain and one，*GSTe*2-2，encodes an enzyme that has the highest levels of DDT dehydrochlorinase activity ever observed and is able to metabolize DDT （Ortelli *et al*.，2003）. It has been found that the overexpression of the Epsilon class of *GSTs* in resistant *A*. *gambiae* is regulated by both *cis*- and *trans*-acting factors （Ranson *et al*.，2000）.

GSTs are responsible for many cases of organophosphate resistance （Hayes and Wolf，1988）. Four different GST genes，*MdGST*-1，-2，-3，and -4，were isolated and sequenced from a house fly Cornell-R strain，which was resistant to OP and carbamate insecticides. Among these four GST isozymes，MdGST-3 was thought more likely to be responsible for OP resistance in the Cornell-R strain （Syvanen *et al*.，1996） through gene amplification and the divergence of sequences among the amplified copies （Syvanen *et al*.，1994；Zhou and Syvanen，1997）. Another GST isozyme，MdGST-6A，was purified from a house fly strain，Cornell-HR，which was highly resistant to OP insecticides. The high insecticide-conjugation activity of MdGST-6A suggests that it plays a significant role in OP resistance in Cornell-HR （Wei *et al*.，2001）. Four GST isozymes，GST-1，GST-2，GST-3，GST-4 were characterized in the diamondback moth *Plutella xylostella* （Chiang and Sun，1993；Ku *et al*.，1994）. Recombinant GST enzymes from the diamondback moth catalyze the conjugation of glutathione to OP insecticides，verifying their role in the detoxification of organophosphate insecticides （Huang *et al*.，1998；Wei *et al*.，2001）.

The correlation of high levels of GST activities with high levels of resistance to pyrethroid has been identified in *Aedes aegypti* （Grant and Matsumura，1989），*Tribolium castaneum* （Reidy *et al*.，1990），and *Spodoptera littoralis* （Lagadic *et al*.，1993）. Although GSTs have not yet been proved to be responsible for the direct metabolism of pyrethroid insecticides （Enayati *et al*.，2005），their role in pyrethroid resistance through detoxifying lipid peroxidation products induced by pyrethroids has been recognized （Vontas *et al*.，2001）.

5 CONCLUSIONS

Efforts to control insect pests that are agriculturally，economically，and medically important often focus on the use of insecticides. However，insects have successfully adapted to most insecticides by becoming physiologically or behaviorally resistant to them. A better understanding of insecticide resistance mechanisms，therefore，will enable us not only to develop a successful program for overcoming resistance，but also to design novel strategies to prevent，or minimize the spread and evolution of resistance.

References

Anspaugh DD，Rose RL，Koehler PG，Hodgson E，Roe RM，1994. Multiple mechanisms of pyrethroid resistance in the German cockroach，*Blattella* *germanica*（L.）. *Pestic*. *Biochem*. *Physiol*.，50：138 – 148.

Argentine JA，Lee SH，Sos MA，Barry S，Clark JM，1995. Permethrin resistance in a near isogenic strain of Colorado potato beetle. *Pestic*. *Biochem*. *Physiol*.，53：97 – 115.

Brown AWA，Pal P，1971. The nature and characterization of resistance. In：Brown AWA，Pal R eds. Insecticide Resistance in Arthropods. World Health Organization，Geneva. 9 – 52.

Bues R，Bouvier JC，Boudinhon L，2005. Insecticide resistance and mechanisms of resistance to selected strains of *Heliciverpa armigera*（Lepidoptera：Noctuidae）in the soeth of France. *Crop Protection*，24：814 – 820.

Campbell PM，Newcomb RD，Russell RJ，Oakeshott JG，1998. Two different amino acid substitutions in the ali-esterase，E3，confer alternative types of organophosphorus insecticide resistance in the sheep blowfly *Lucilia cuprina*. *Insect Biochem*. *Molec*. *Biol*.，28：139 – 150.

Carino FA，Koener JF，Plapp FW，Jr Feyereisen R，1994. Constitutive overexpression of the cytochrome P450 gene *CYP6A*1 in a house fly strain with metabolic resistance to insecticides. *Insect Biochem*. *Molec*. *Biol*.，24：411 – 418.

Chen Z，Newcomb R，Forbes E，McKenzie J，Batterham P，2001. The acetylcholinesterase gene and organophosphorus resistance in the Australian sheep blowfly，*Lucilia cuprina*. *Insect Biochem*. *Molec*. *Biol*.，31：805 – 816.

Chen WL，Sun C，1994. Purification and characterization of carboxylesterases of a rice brown planthopper，*Nilaparvata lugens* Stål. *Insect Biochem*. *Molec*. *Biol*.，24：347 – 355.

Chiang FM，Sun CN，1993. Glutathione transferase isozymes of diamondback moth larvae and their role in the degradation of some organophosphorus insecticides. *Pest*. *Biochem*. *Physiol*.，45：7 – 14.

Chris B，Iris S，Andreas T，Linda MF，Martin SW，2004. Identification of mutations associated with pyrethroids resistance in the para-type sodium channel of the cat flea，*Ctenocephalides felis*. *Insect Biochem*. *Molec*. *Biol*.，34：1 305 – 1 313.

Claudianos C，Russell RJ，Oakeshott JG，1999. The same amino acid substitution in orthologous esterases confers organophosphate resistance on the house fly and a blowfly. *Insect Biochem*. *Mol*. *Biol*.，29：675 – 686.

Cuany A，Handani J，Berge J，Fournier D，Raymond M，Georghiou GP，Pasteur N，1993. Action of esterase B1 on chlorpyrifos in organophosphate-resistant *Culex* mosquitoes. *Pestic*. *Biochem*. *Physiol*.，45：1 – 6.

Daborn P，McCart C，Woods D，Ffrench-Constant RH，2004. Detection of insecticide resistance-associated mutations in cat flea *Rdl* by TaqMan-allele specific amplification. *Pestic*. *Biochem*. *Physiol*.，79：25 – 30.

Daborn PJ，Yen JL，Bogwitz MR，Le Goff G，Feil E，Jeffers S，Tijet N，Perry T，Heckel D，Batterham P，Feyereisen R，2002. A single P450 allele associated with insecticide resistance in *Drosophila*. *Science*，297：2 253 – 2 256.

Devonshire AL，Field LM，Foster SP，Moores GD，Williamson MS，Blackman RL，1998. The evolution of insecticide resistance in the peach-potato aphid，*Myzus persicae*. *Philos*. *Trans*. *R*. *Soc*. *Lond*. *B*. *Biol*. *Sci*.，353：1 677 – 1 684.

Devonshire AL，Moores GD，1982. A carboxylesterase with broad substrate specificity causes organophosphorus，carbamate and pyrethroid resistance in peachpotato aphids（*Myzus persicae*）. *Pestic*. *Biochem*. *Physiol*.，18：235 – 246.

DeVries DH，Georghiou GP，1981. Decreased nerve sensitivity and decreased cuticular penetration as mechanisms of resistance to pyrethroids in a（1R）-*trans*-permethrin selected strain of the house fly. *Pestic*. *Biochem*. *Physiol*.，15：234 – 241.

Eldefrawi ME，Miskus R，Sutcher V，1960. Methylenedioxyphenyl derivatives as synergists for carbamate insecticides on susceptible，DDT- and parathion-resistant house flies. *J*. *Econ*. *Entomol*.，53：231 – 234.

Enayati AA，Ranson H，Hemingway J，2005. Insect glutathione transferases and insecticide resistance. *Insect*. *Mol*. *Biol*.，14：3 – 8.

Farnham AW，1973. Genetics of resistance of pyrethroid-selected houseflies，*Musca domestica* L. *Pestic*. *Sci*.，4：513 – 520.

Ferrari JA，Georghiou GP，1990. Esterase Bi activity variation within and among insecticide resistant，susceptible，and heterozygous strains of *Culex quinquefasciatus*（Diptera：Culicidae）. *J*. *Econ*. *Entomol*.，83：1 704 – 1 710.

Feyereisen R，1995. Molecular biology of insecticide resistance. *Toxicol*. *Lett*.，82：83 – 90.

Feyereisen R，1999. Insect P450 enzymes. *Annu*. *Rev*. *Entomol*.，44：507 – 533.

Feyereisen R，Andersen JF，Carino FA，Cohen MB，Koener JF，1995. Cytochrome P450 in the house fly：structure，catalytic activity and regulation of expression of *CYP6A*1 in an insecticide-resistant strain. *Pestic*. *Sci*.，43：233 – 239.

Feyereisen R，Koener JF，Farnsworth DE，Nebert DW，1989. Isolation and sequence of cDNA encoding a cytochrome P450 from an insecticide-resistant strain of the house fly，*Musca domestica*. *Proc*. *Natl*. *Acad*. *Sci*. *USA*，86：1 465 – 1 469.

Ffrench-Constant RH，Daborn PJ，Le Goff G，2004. The genetics and genomics of insecticide resistance. *Trends in Genetics*，20：163 – 170.

Fournier D，Bride JM，Poire M，Berge JB，Plapp FW，1992. Insect glutathione S-transferases. Biochemical characteristics of the major forms from houseflies susceptible and resistant to insecticides. *J*. *Biol*. *Chem*.，267（3）：1 840 – 1 845.

Gao J，Zhu KY，2000. Comparative toxicity of selected organophosphate insecticides against resistant and susceptible clones of the greenbug，*Schizaphis graminum*（Homoptera：Aphididae）. *J*. *Agri*. *Food Chem*.，48：4 717 – 4 722.

Georghiou GP，1971. Isolation，characterization and re-synthesis of insecticide resistance factors in the house fly，*Musca domestica*. In：Proc. 2nd Internat. Cong. Pestic. Chem. 2. 77 – 94.

Georghiou GP，1972. The evolution of resistance to pesticides. *Annu*. *Rev*. *Ecol*. *Syst*.，3：133 – 168.

Georghiou GP，1980. Implications of the development of resistance to pesticide：basic principles and consideration of countermeasures. In：Gooding EGBed. Proceedings of Pest and Pesticide Management. Caribbean. 116 – 132.

Georghiou GP，1986. The magnitude of the resistance problem. In：National Academy of Sciences ed. Pest Resistance Strategies and Tactics for Management. National Academy Press，Washington，D.C. 14 – 43.

Georghiou GP，Lagunes-Tejeda A，1991. The Occurrence of Resistance to Pesticides in Arthropods. Food and Agriculture Organization of the United Nations，Rome.

Georghiou GP，Mellon RB，1983. Pesticide resistance in time and space. In：Georghiou GP，Saito T eds. Pest Resistance to Pesticides. Plenum Press，New York. 1 – 46.

Goh DKS，Anspaugh DD，Motoyama N，Rock GC，Roe RM，1995. Isolation and characterization of an insecticide-resistance-associated esterase in the tobacco budworm，*Heliothis virescens*（F.）. *Pestic*. *Biochem*. *Physiol*.，51：192 – 204.

Granados RR，Fu Y，Corsaro B，Hughes PR，2001. Enhancement of *Bacillus thuringiensis* toxicity to Lepidopterous species with the enhancing from *Trichoplusia ni* granulovirus. *Biol*. *Control*，20：153 – 159.

Grant DF，Dietze EC，Hammock BD，1991. Glutathione S-transferase isozymes in *Aedes aegypti*：purification，characterization and isozyme-specific regulation. *Insect Biochem*.，4：421 – 433.

Grant DF，Hammock BD，1992. Genetic and molecular evidence for a trans-acting regulatory locus controlling glutathione S-transferase-2 expression in *Aedes aegypti*. *Mol*. *Gen*. *Genet*.，234：169 – 176.

Grant DF，Matsumura F，1989. Glutathione S-transferase 1 and 2 in susceptible and insecticide resistant *Aedes aegypti*. *Pestic*. *Biochem*. *Physiol*.，33：132 – 143.

Gunning RV，Moores GD，Devonshire AL，1996. Esterases and esfenvalerate resistance in Australian *Helicoverpa armigera*（Hübner）（Lepidoptera：Noctuidae）. *Pestic*. *Biochem*. *Physiol*.，54：12 – 23.

Guo HL，Gao XW，2005. The mutation of carboxylesterase gene of cotton aphid，*Aphis gossypii* associated with omethoate resistance. *Acta Entomologica Sinica*，48（2）：194 – 202.

Hayes JD，Wolf CR，1988. Role of glutathione transferase in drug resistance. In：Sies H，Ketterer B eds. Glutathione Conjugation：Mechanisms and Biological Significance. Academic Press Ltd，London. 315 – 355.

Hemingway J，2000. The molecular basis of two contrasting metabolic mechanisms of insecticide resistance. *Insect Biochem*. *Mol*. *Biol*.，30：1 009 – 1 015.

Hemingway J，Hawkes NJ，McCarroll L，Ranson H，2004. The molecular basis of insecticide resistance in mosquitoes. *Insect Biochem*. *Mol*. *Biol*.，34：653 – 665.

Hemingway J，Karunaratne SHPP，1998. Mosquito carboxylesterases：a review of the molecular biology and biochemistry of a major insecticide resistance mechanism. *Med*. *Vet*. *Entomol*.，12：1 – 12.

Hemingway J，Ranson H，2000. Insecticide resistance in insect vectors of human disease. *Annu. Rev. Entomol.*，45：371 – 392.

Hemingway J，Hawkes NJ，McCarroll L，Ranson H，2004. The molecular basis of insecticide resistance in mosquitoes. *Insect Biochem. Molec. Biol.*，34：653 – 665.

Huang HS，Hu NT，Yao YE，Wu CY，Chiang SW，Sun CN，1998. Molecular cloning and heterologous expression of a glutathione S-transferase involved in insecticide resistance from the diamondback moth，*Plutella xylostella*. *Insect Biochem. Molec. Biol.*，28：651 – 658.

Karunarantne SHPP，Hemingway J，2000. Insecticide resistance spectra and resistance mechanisms in populations of Japanese encephalitis vector mosquitoes，*Culex tritaeniorhynchus* and *Cx. gelidus*，in Sri Lanka. *Med. Vet. Entomol.*，14：430 – 436.

Karunaratne SHPP，Jayawardena KGI，Hemingway J，Ketterman AJ，1993. Characterization of a B-type esterase involved in insecticide resistance from the mosquito *Culex quinquefasciatus*. *Biochem. J.* 294：575 – 579.

Kasai S，Weerashinghe IS，Shono T，Yamakawa M，2000. Molecular cloning，nucleotide sequence and gene expression of a cytochrome P450（CYP6F1）from the pyrethroid-resistant mosquito，*Culex quinquefasciatus* Say. *Insect Biochem. Molec. Biol.*，30：163 – 171.

Ketterman AJ，Jayawardena KG，Hemingway J，1992. Purification and characterization of a carboxylesterase involved in insecticide resistance from the mosquito *Culex quinquefasciatus*. *Biochem. J.*，287：355 – 360.

Konno Y，Shishido T，1989. Binding protein，a factor of fenitroxon detoxification in OP-resistant rice stem borers. *J. Pestic. Sci.*，14：359 – 362.

Kostaropoulos I，Papadopoulos AI，Metaxakis A，Boukouvala E，Papadopoulou-Mourkidou E，2001. Glutathione S-transferase in the defence against pyrethroids in insects. *Insect Biochem. Molec. Biol.*，31：313 – 319.

Ku CC，Chiang FM，Hsin CY，Yao YE，Sun CN，1994. Glutathione transferase isozymes involved in insecticide resistance of diamondback moth larvae. *Pestic. Biochem. Physiol.*，50：191 – 197.

Lagadic L，Cuany A，Berge JB，Echaubard M，1993. Purification and partial characterization of glutathione S-transferases from insecticide-resistant and lindaneinduced susceptible *Spodoptera littoralis*（Boisd.）larvae. *Insect Biochem. Molec. Biol.*，23：467 – 474.

Lee S，Clark JM，1996. Tissue distribution and biochemical characterization of carboxylesterases associated with permethrin resistance in a near isogenic strain of Colorado potato beetle. *Pestic. Biochem. Physiol.*，56：208 – 219.

Lee SH，Clark JM，1998. Permethrin carboxylesterase functions as nonspecific sequestration proteins in the hemolymph of Colorado potato beetle. *Pestic. Biochem. Physiol.*，62：51 – 63.

Leng XF，Tang ZH，Wang YC，1996. Molecular Toxicology of Insecticides and Insect Resistance. Beijing：China Agriculture Press. 1 – 171.

Liu N，Scott JG，1996. Genetic analysis of factors controlling elevated cytochrome P450，CYP6D1，cytochrome b5，P450 reductase and monooxygenase activities in LPR house flies，*Musca domestica*. *Biochem. Genet.*，34：133 – 148.

Liu N，Scott JG，1998. Increased transcription of *CYP6D1* causes cytochrome P450-mediated insecticide resistance in house fly. *Insect Biochem. Molec. Biol.*，28：531 – 535.

Liu N，Yue X，2000. Insecticide resistance and cross-resistance in the house fly（Diptera：Muscidae）. *J. Econ. Entomol.*，93：1 269 – 1 275.

Liu YJ，Shen JL，2003. Cuticular penetration mechanism of resistance to lambda-cyhalothrin in *Spodoptera exigua*（Hübner）. *Acta Entomologica Sinica*，46（3）：288 – 291.

Lockwood JA，Byford RL，Story RN，Sparks TC，Quisenberry SS，1985. Behavioral resistance to the pyrethroids in the horn fly，*Haematobia irritans*（Diptera：Muscidae）. *Environ. Entomol.*，14：873 – 880.

Mathenge EM，Gimnig JE，Kolczak M，Ombok M，Irungu LW，Hawley WA，2001. Effect of permethrin-impregnated nets on exiting behaviour，blood feeding success，and time of feeding of malaria mosquitoes（Diptera：Culicidae）in Western Kenya. *J. Med. Entomol.*，38：531 – 536.

Mbogo CNM，Baya NM，Ofulla AVO，Githure JI，Snow RW，1996. The impact of permethrin-impregnated bednets on malaria vectors of the Kenyan coast. *Med. Vet. Entomol.*，10：251 – 259.

Moulton JK，Pepper DA，Dennehy TJ，2000. Beet armyworm（*Spodoptera exigua*）resistance to spinosad. *Pest Manag. Sci.*，56：842 – 848.

Natsuhara K，Shimada K，Tanaka T，Miyata T，2004. Phenobarbital induction of permethrin detoxification and phenobarbital metabolism in susceptible and resistant strains of the beet armyworm *Spodoptera exigua*（Hübner）. *Pestic. Biochem. Physiol.*，79：33 – 41.

Newcomb RD，Campbell PM，Ollis DJ，Cheah E，Russell RJ，Oakeshott JG，1997a. A single amino acid substitution converts a carboxylesterase to an organophosphorus hydrolase and confers insecticide resistance on a blowfly. *Proc. Natl. Acad. Sci. USA*，94：7 464 – 7 468.

Newcomb RD，Campbell PM，Russell RJ，Oakeshott JG，1997b. cDNA cloning，baculovirus-expression and kinetic properties of the esterase，E3，involved in organophosphorus resistance in *Lucilia cuprina*. *Insect Biochem. Mol. Biol.*，27：15 – 25.

Nikou D，Ranson H，Hemingway J，2003. An adult-specific CYP6 P450 gene is overexpressed in a pyrethroid-resistant strain of the malaria vector，*Anopheles gambiae*. *Gene*，318：91 – 102.

Oppenoorth FJ，1985. Biochemistry and genetics of insecticide resistance. In：Kerkut GA，Gilbert LI eds. Comprehensive Insect Physiology Biochemistry and Pharmacology. Pergamon Press，Oxford. 731 – 773.

Ortelli F，Rossiter LC，Vontas J，Ranson H，Hemingway J，2003. Heterologous expression of four glutathione transferase genes genetically linked to a major insecticide-resistance locus from the malaria vector *Anopheles gambiae*. *Biochem. J.*，373：957 – 963.

Ottea JA，Younis IAM，Young RJ，Leonard BR，McCaffery AR，1995. Biochemical and physiological mechanisms of pyrethroid resistance in *Heliothis virescens*（F.）. *Pestic. Biochem. Physiol.*，51：117 – 128.

Pan WL，Dang ZH，Gao ZL，2003. Comparison of activities of detoxifying enzymes in the imidacloprid-resistant and susceptible strains of the cotton aphid，*Aphis gossypii*. *Acta Entomologica Sinica*，46（6）：793 – 796.

Perez-Mendoza J，Fabrick JA，Zhu KY，Baker JE，2000. Alterations in esterases are associated with malathion resistance in *Habrobracon hebetor*（Hymenoptera：Braconidae）. *J. Econ. Entomol.*，93：31 – 37.

Pittendrigh B，Aronstein K，Zinkovsky E，Andreev O，Bronwyn C，Daly J，Trowell S，Ffrench-Constant RH，1997. Cytochrome P450 genes from *Helicoverpa armigera*：expression in a pyrethroid-susceptible and -resistant strain. *Insect Biochem. Molec. Biol.*，27：507 – 512.

Plapp FW Jr，Hoyer RF，1968. Insecticide resistance in the house fly：decreased rate of absorption as the mechanism of action of a gene that acts as an intensifier of resistance. *J. Econ. Entomol.*，61：1 298 – 1 303.

Prabhakaran SK，Kamble ST，1995. Purification and characterization of an esterase isozyme from insecticide resistant and susceptible strains of German cockroach，*Blattella germanica*（L.）. *Insect Biochem. Molec. Biol.*，25：519 – 524.

Prapanthadara L，Hemingway J，Ketterman AJ，1993. Partial purification and characterization of glutathione S-transferase involved in DDT resistance from the mosquito *Anopheles gambiae*. *Pest. Biochem. Physiol.*，47：119 – 133.

Prapanthadara L，Koottathep S，Promtet N，Hemingway J，Ketterman AJ，1996. Purification and characterization of a major glutathione S-transferase from the mosquito *Anopheles dirus*（Species B）. *Insect Biochem. Molec. Biol.*，26：277 – 285.

Pridgeon JW，Zhang L，Liu N，2003. Overexpression of CYP4G19 associated with a pyrethroid-resistant stain of the German cockroach，*Blattella germanica*（L.）. *Gene*，314：157 – 163.

Ranson H，Jensen B，Wang X，Prapanthadara L，Hemingway J，Collins FH，2000. Genetic mapping of two loci affecting DDT resistance in the malaria vector，*Anopheles gambiae*. *Insect Mol. Biol.*，9：499 – 507.

Ranson H，Rossiter L，Ortelli F，Jensen B，Wang X，Roth CW，Collins FH，Hemingway J，2001. Identification of a novel class of insect glutathione S-transferases involved in resistance to DDT in the malaria vector *Anopheles gambiae*. *Biochem. J.*，359：295 – 304.

Raymond M，Chevillon C，Guillemaud T，Lenormand T，Pasteur N，1998. An overview of the evolution of overproduced esterases in the mosquito *Culex pipiens*. *Philos. Trans. R. Soc. Lond. B. Biol. Sci.*，353：1 707 – 1 711.

Reidy GF，Rose HA，Visetson S，Murray M，1990. Increased glutathione S-transferase activity and glutathione content in an insecticide-resistant strain of *Tribolium castaneum*（Herbst）. *Pestic. Biochem. Physiol.*，36：269 – 276.

Ross MH，1992. Difference in the response of German cockroach（Dictyoptera：Blattellidae）field strains to vapors of pyrethroid formulations. *J. Econ. Entomol.*，85：123 – 129.

Ross MH，1997. Evolution of behavioral resistance in German cockroaches（Dictyoptera：Blattellidae）. *J. Econ. Entomol.*，90：1 482 – 1 485.

Ross MH，1998. Response of behaviorally resistant German cockroaches（Dictyoptera：Blattellidae）to the active ingredient in a commercial bait. *J. Econ. Entomol.*，91：150 – 152.

Salinas AE，Wong MG，1999. Glutathione S-transferases – a review. *Current*

Med. *Chem*.，6∶279 – 309.

Sawicki RM，1970. Interaction between the factor delaying penetration of insecticides and the demethylation mechanisms of resistance to organophosphorus-resistant house flies. *Pestic*. *Sci*.，1∶84 – 87.

Scharf ME，Hemingway J，Small GJ，Bennett GW，1997. Examination of esterases from insecticide resistant and susceptible strains of the German cockroach，*Blattella germanica*（L.）. *Insect Biochem*. *Molec*. *Biol*.，27∶489 – 497.

Scharf ME，Meinke LJ，Wright RJ，Chandler LD，Siegfried BD，1999. Metabolism of carbaryl by insecticide-resistant and -susceptible western corn rootworm populations（Coleoptera∶Chrysomelidae）. *Pestic*. *Biochem*. *Physiol*.，63∶85 – 96.

Scott JG，1989. Cross-resistance to the biological insecticide abamectin in pyrethroid resistant house flies. *Pestic*. *Biochem*. *Physiol*.，34∶27 – 31.

Scott JG，1991. Insecticide resistance in insects. In∶Pimental D ed. Handbook of Pest Management. CRC Press，Boca Raton. 663 – 677.

Scott JG，1999. Cytochrome P450 and insecticide resistance. *Insect Biochem*. *Molec*. *Biol*.，29∶757 – 777.

Scott JG，Georghiou GP，1986a. Mechanisms responsible for high levels of permethrin resistance in the house fly. *Pestic*. *Sci*.，17∶195 – 206.

Scott JG，Georghiou GP，1986b. The biochemical genetics of permethrin resistance in the Learn-PyR of house fly. *Biochem*. *Genet*.，24∶25 – 37.

Scott JG，Liu N，Wen Z，1998. Insect cytochrome P450∶diversity，insecticide resistance and tolerance to plant toxins. *Comp*. *Biochem*. *Physiol*.，121C∶147 – 155.

Scott JG，Wen Z，2001. Cytochromes P450 of insects∶the tip of the iceberg. *Pest Manag*. *Sci*.，57∶958 – 967.

Silverman J，Bieman DN，1993. Glucose aversion in the German cockroach，*Blattella germanica*. *Insect Physiol*.，39∶925 – 933.

Small GJ，Hemingway J，2000. Molecular characterization of the amplified carboxylesterase gene associated with organophosphorus insecticide resistance in the brown planthopper，*Nilaparvata lugens*. *Insect Mol*. *Biol*.，9∶647 – 653.

Small GJ，Karunaratne SHPP，Hemingway J，1998. Characterization of amplified esterase Estβ12 associated with organophosphate resistance in a multi-resistant population of the mosquito *Culex quinquen fasciatus* from Cuba. *Med*. *Vet*. *Entomol*.，12∶187 – 191.

Sonoda S，Tsumuki H，2005，Studies on glutathione S-transferase gene involved in chlorfluazuron resistance of the diamondback moth，*Plutella xylostella* L.（Lepidoptera∶Yponomeutidae）. *Pestic*. *Biochem*. *Physiol*.，82∶94 – 101.

Sparks TC，Lockwood JA，Byford RL，Graves JB，Leonard BR，1989. The role of behavior in insecticide resistance. *Pestic*. *Sci*.，26∶383 – 399.

Syvanen M，Zhou ZH，Wang JY，1994. Glutathione transferase gene family from the housefly *Musca domestica*. *Mol*. *Gen*. *Genet*.，245∶25 – 31.

Syvanen M，Zhou Z，Wharton J，Goldsbury C，Clark A，1996. Heterogeneity of the glutathion transferase genes encoding enzymes responsible for insecticide degradation in the housefly. *J*. *Mol*. *Evol*.，43∶236 – 240.

Tabashnik BE，Johnson KW，Engleman JT，Baum JA，2000. Cross-resistance to *Bacillus thuringiensis* toxin Cry1Ja in a strain of diamondback moth adapted to artificial diet. *J*. *Invertebrate Pathol*.，76∶81 – 83.

Tang ZH，Bi Q，2003. Molecular Behavior of Insecticide Action. Shanghai∶Shanghai Far East Publishing House. 1 – 675.

Tomita T，Scott JG，1995. cDNA and deduced protein sequence of *CYP6D1*∶the putative gene for a cytochrome P450 responsible for pyrethroid resistance in house fly. *Insect Biochem*. *Molec*. *Biol*.，25∶275 – 283.

Townsend MG，Busvine JR，1969. The mechanism of malathion resistance in the blowfly *Chrysomya putoria*. *Entomol*. *Exp*. *Appl*.，12∶243 – 267.

Valles SM，Dong K，Brenner RJ，2000. Mechanisms responsible for cypermethrin resistance in a strain of German cockroach，*Blattella germanica*. *Pestic*. *Biochem*. *Physiol*.，66∶195 – 205.

van Asperen K，Oppenoorth FJ，1959. Organophosphate resistance and esterase activity in house flies. *Entomol*. *Exp*. *Appl*.，2∶48 – 57.

Vontas JG，Small GJ，Hemingway J，2000. Comparison of esterase gene amplification，gene expression and esterase activity in insecticide susceptible and resistant strains of the brown planthopper，*Nilaparvata lugens*（Stål）. *Insect Mol*. *Biol*.，9∶655 – 660.

Vontas JG，Small GJ，Hemingway J，2001. Glutathione S-transferases as antioxidant defense agents confer pyrethroid resistance in *Nilaparvata lugens*. *Biochem*. *J*.，357∶65 – 72.

Waters LC，Zelhof AC，Shaw BJ，Chang LY，1992. Possible involvement of the long terminal repeat of transposable element 17.6 in regulating expression of an insecticide resistance-associated P450 gene in *Drosophila*. *Proc*. *Natl*. *Acad*. *Sci*. *USA*，89∶4 855 – 4 859.

Wheelock GD，Scott JG，1989. Simultaneous purification of a cytochrome P-450 and cytochrome b5 from the house fly *Musca domestica* L. *Insect Biochem*.，19∶481 – 488.

Wei Y，Appel AG，Moar WJ，Liu L，2001. Pyrethroid resistance and cross resistance in the German cockroach，*Blattella germanica*（L.）. *Pest Manag*. *Sci*.，57∶1 055 – 1 059.

Wei SH，Clark AG，Syvanen M，2001. Identification and cloning of a key insecticide-metabolizing glutathione S-transferase（MdGST-6A）from a hyper insecticide-resistant strain of the housefly *Musca domestica*. *Insect Biochem*. *Molec*. *Biol*.，31∶1 145 – 1 153.

Wen Z，Scott JG，1999. Genetic and biochemical mechanisms limiting fipronil toxicity in the LPR strain of house fly，*Musca domestica*. *Pestic*. *Sci*.，55∶988 – 992.

Whyard S，Downe AER，Walker VK，1995. Characterization of a novel esterase conferring insecticide resistance in the mosquito *Culex tarsalis*. *Arch*. *Insect Biochem*. *Physiol*.，29∶329 – 342.

World Health Organization，1957. Expert Committee on Insecticides. WHO Tech. Rpt. Ser. 7th Rpt. 125.

Wu D，Scharf ME，Neal JJ，Suiter DR，Bennett GW，1998. Mechanisms of fenvalerate resistance in the German cockroach，*Blattella germanica*（L.）. *Pestic*. *Biochem*. *Physiol*.，61∶53 – 62.

Yang Y，Wu Y，Chen S，Devine GJ，Denholm I，Jewess P，Moores GD，2004，The involvement of microsomal oxidases in pyrethroid resistance in *Heliciverpa armigera* from Asia. *Insect Biochem*. *Molec*. *Biol*.，34∶763 – 773.

Zhao G，Liu W，Knowles CO，1994. Mechanisms associated with Diazinon resistance in western flower thrips. *Pestic*. *Biochem*. *Physiol*.，49∶13 – 23.

Zhou ZH，Syvanen M，1997. A complex glutathione transferase gene family in the house fly，*Musca domestica*. *Mol*. *Gen*. *Genet*.，256∶187 – 194.

Ziegler R，Whyard S，Downe AER，Wyatt GR，Walker VK，1987. General esterase，malathion carboxylesterase and malathion resistance in *Culex tarsalis*. *Pestic*. *Biochem*. *Physiol*.，28(2)∶279 – 285.

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昆虫抗药性机理：行为和生理改变及解毒代谢增强

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摘要：杀虫剂抗性是指‘生物的一个品系发展了对该生物正常种群中大多数个体具有致死作用剂量的杀虫药剂的能力”。行为改变、生理学上的变化或代谢解毒等抗性机制能够降低毒物到达靶标的有效剂量。行为抗性是指减少昆虫与毒物接触或使昆虫能够存活于对大多数对正常个体致死（或有害）的环境中的任何行为。生理学改变的机制包括杀虫剂对表皮的穿透性降低、增加对药剂阻隔（sequestration）或储存和加速杀虫剂的排泄。细胞色素P450、水解酶和谷胱甘肽S-转移酶是杀虫药剂代谢解毒的主要3大酶系。细胞色素P450是一个超基因家族，是生物体内对外源性和内源性化合物解毒代谢或活化最重要的酶系。在许多害虫中发现P450介导的解毒代谢增加导致了对杀虫药剂抗性的增加。谷胱甘肽S-转移酶是可溶性的二聚体蛋白，与代谢解毒、大量内源性和外源性化合物的排泄有关，许多昆虫中证明其抗药性与该酶活性增加有关。水解酶实际上是一组异源的酶类，其对抗药性的作用包括通过基因扩增增加酶量，作为结合蛋白隔离杀虫药剂或通过增加酶的活性加强对药剂的水解作用。

关键词：杀虫剂抗药性；行为改变；生理变化；解毒代谢；谷胱甘肽S-转移酶；细胞色素P450

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